**LFTs Webinar Transcript.**

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0:01 **Chair:** Good afternoon and welcome to our live webinar on how to approach abnormal liver function tests. So, without further ado I'd like to introduce our speaker today Dr Ian Rees who is a consultant gastroenterologist for Hywel Dda health board. He has particular expertise on liver disease and he's going to update us now on how best to approach liver function tests. Thank you, Ian.

0:34 **Speaker:** Thank you, Nicola. The title that has been given to me isn't the title I would have chosen and hopefully I’ll explain that as we go along. So, the title I’ve chosen is ‘approach to abnormal liver tests’ and you'll notice there's one word that's missing and hopefully during my talk you'll come to see why I’ve left that letter out. So, I think what I’m going to try and convey to you is my personal feelings. I was slightly reluctant to give this talk because I appreciate the audience is from around Wales and there are my ideas and the all-Wales ideas, and they're not always the same. So, I’ve tried to give a party line on this but also with some slight changes.

1.16 **Speaker:** So, I’m going to talk about

* what are liver function tests? (I’ve used the word liver function test hopefully that'll be the only time that that appears there)
* which tests are useful and for what?
* how do we interpret them?
* I have put some guidelines on which I think this talk is always asked for, because the guidelines are confusing contradictory and multiple
* there are some cases, but to be honest with you I don't think we'll have time for the cases. But if we do, we can. They're just simple stuff really that we come across routinely.

1:46 **Speaker:** So, what we call liver function tests are not really liver function tests. They are liver tests. So, what do we measure? We measure things like ALT, AST (so they're the transaminases really), Alkaline Phosphatase, Gamma GT, Bilirubin. But they're not really functioning tests. They're not measures of the functioning of the liver. They are tests associated with the liver and associated with many other things. If you ask me which, if I wanted to assess my liver function at this moment, I would ask for an Albumin and a Prothrombin time. That would be a far more useful answer as to whether my liver is functioning well. So that's why the move away from the term liver function test. Although I appreciate it still appears on the clinical portal as that.

2:30 **Speaker:** So, these transaminases then, the ALT and the AST, generally we associate them with hepatocyte damage. One thing I will draw your attention to, is normal ranges. We feel (and the ‘royal we’) feel that 30 for men and 18 for women would be normal. Now depending on where you work in Wales, I’ve seen levels of up to 50 being normal and certainly I’ve seen plenty of patients with significant liver disease with so-called ‘normal’ transaminases. So, there's one issue - they're probably not great at measuring liver function; also depending on the normal range, you can have a disease and equally the opposite is true, you can have abnormal liver tests with no disease.

3.20 **Speaker:** So, these things are different. So, I often say to people - you know a teenager should have maybe an ALT of maybe no more than their years in age. You know, sort of 17/18, something like that. And many patients who have viral hepatitis will have normal range ALTs. So, these are obviously useful of course and we use them all the time, but I think what I’m trying to convey to you is they need to be interpreted with caution. Many people with liver test abnormalities, actually when we do biopsy them, have very little to find.

3:54 **Speaker:** Now one of the banes of my life is when a GP WCP referral comes through without raised alkaline phosphates and my heart sinks because to be honest with you this is very common. I try and bat it to somebody else because obviously it's so non-specific, but usually I have to take it on. So alkaline phosphate is very commonly abnormal, and I would say more commonly than not associated with other stuff, other than the liver. Obviously in general practice you'll see more pregnant people than I do but the placenta produces alkaline phosphatase, bone produces alkaline phosphatase. There's a huge variation in age. It can certainly reflect biliary disease and cholestasis of course it can, and in the only setting I find it useful at all, a Gamma GT can be useful in helping there. I used to ask for Isoenzymes, but I tend to find that the laboratory blocks that, and tends to suggest a Gamma GT.

4:50 **Speaker:** So, I don't use Gamma GT at all. I see a lot of people in primary care and in substance misuse they're big fans of the Gamma GT. It's not now a routine liver test. It used to be back in the days of the smack, and if any of you remember smack, it used to be this biochemistry thing that gave you everything. The problem is it goes up with the wind; it goes up in anything and everything and can be you know very, very non-specific. The only place I find it of use is if I have a raised alkaline phosphatase, then a Gamma GT*may* help. I’m saying *may* because obviously if alkaline phosphate is up due to inflammation and the Gamma GT may be up as well. People often use it as a measure of alcohol misuse. I don't really. And it is apparently the most common liver test abnormality in non-alcoholic fatty liver. So, it's a pretty useless test. But I do see a lot of people in non-liver practices use it.

5:55 **Speaker:** So, the other one is Bilirubin. Obviously, a major liver test. It can look at hepatocellular damage of cholestasis but there are lots of other things. At least seven to half a dozen referrals a year reflect Gilbert Syndrome (so isolated raised Bilirubin) certain drugs e.g. Fusidic acid. You get isolated Bilirubin anaemia. But it is a measure in many ways of hepatocellular damage and cholestasis. Those I think are what I would call liver tests - the ALT and AST, the alkaline phosphatase, the Bilirubin, and the Gamma GT. I don't use Gamma GT.

6:35 **Speaker:** So, these are the things on the ward and in the clinic that I would really be looking at and so I’d probably add the Bilirubin to this as well. So, the Albumin. Again, it's not specific. You can go in other things, but certainly it's a good idea if your liver is not working well, you're out in the outpatient clinic an Albumin of 24 and you think ‘oh there's something not right here’. Obviously if you're in the hospital and someone's had burns, or you've got a nephrotic syndrome, or you've got gut failure of course, you know they're more obvious. But in the right setting the Albumin is a really nice measure. With these graphs we get on the Welsh Clinical Portal now, you can often track the Albumin dropping down over a protracted period. And then Prothrombin time or INR is again very useful. There's lots of confounding factors of course if you've got cholestasis or if you've got warfarin or even the DOACs. I don't care what they say, DOACs definitely change your clotting string because they're all a bit up. But it is it is a very useful functioning test of your liver.

7:40 **Speaker:** So, I’m milking this point slightly but hopefully the paradox of hepatology's liver function tests do not reflect liver function. I used to use this analogy when I first started. My wife had quite a cronky car, back in the day. It did very well. Many, many happy years but it looked like - it looked bad (I’m very mindful not to swear because I can't see the audience). The car looked awful, but it did very well, and it got her to work and it got the kids to football. So, the paradox is that the car looked awful, but it worked. And that's the paradox of the liver tests in many ways. A liver can look good or the liver tests can look good, but actually underneath it's bad. So that's why I think if you think of this car try and interpret liver tests with caution. I would avoid the term liver function test, although I accept that's what's on the Clinical Portal.

8:36 **Speaker:** So, what's useful? We get lots of referrals and I often find that my colleagues in the hospital who aren't predominantly interested in the liver really are - ‘clueless’ is a wrong word but ‘disinterested’. You often get referred abnormal liver tests, so what you do? So, I think like anything you've got to have a plan and start with the patient not the liver test and I think what you've got to try and do is look at what do these tests mean? What's the ultimate? Does it reflect anything? Does it reflect nothing, and does it reflect any significant underlying liver disease?

9.20 **Speaker:** So, I have presumably confused everybody because we're talking about liver function tests and I said they don't exist. So, think liver tests not liver function tests. Think of non-causes of liver diseases and often this black and white cholestasis versus hepatocellular pattern isn't really that useful. So how do I approach abnormal liver tests? There will be those of you who sigh and those of you who jump for joy when you see that as a physician, that the history is really key. History is really key to explaining abnormal liver tests. The number of times you've had that eureka moment when the patient says, ‘and the doctor gave me Flucloxacillin’ and then you think ‘ah, well that's it’ and so history is absolutely vital. So, with the history you can usually tie things together.

10.10 **Speaker:** I had a young lady now from the Gwendraeth Valley, maybe one of Nicola’s patients, been feeling unwell for a couple of months, non-specific, bit of an ache in the right upper quadrant, transaminases are up. To cut a long story short, she's got autoimmune hepatitis. We often see people then who come in with right upper quadrant discomfort, episodes of nausea at night. So, the history is absolutely vital and absolutely key. So, symptoms - looking for any viral prodrome, any autoimmune sort of feelings. Cholestasis is usually quite easy to spot. Nausea is the top symptom. I think more than pain, people waking up in the middle of the night with really bad nausea and sweating. I’m sure you see this more than I do. People's age is really important. Hepatitis E for example, isn't a middle-aged man's problem. CMV and EBV is a young person's disease. Jobs aren't so important anymore, but obviously you get exposed to stuff, travel and contacts are important. Medications got to be top of the list. So, taking a good history.

We had a woman, again from the Gwendraeth Valley from Pontyates, who'd taken some herbal remedy for her liver and given herself acute liver failure. I think it had some marshmallow root or something, so always ask history, medication, family history, transfusion. Sorry to pick on Pontyberem, but I had a woman from Pontyberem who had UC, had a transfusion in 1988, abnormal liver tests and subsequently turned out to have Hep C. So, these are really important things. You're looking at the symptoms, the chronology, what's been happening, past medical history obviously with regards to probably the most important thing you see, which is non-alcoholic fatty liver. So, looking at co-existent diseases like diabetes.

12.00 **Speaker:** So, examination is useful, but less useful I think than the history. There are obviously the classic signs we all see for chronic liver disease. That's easy. When things are obvious it's easy. I think it's in people who just you find with abnormal liver tests are probably the ones that give us the biggest headache. Cachexia and weight loss associated maybe with cholangiocarcinoma or hetero pancreas cancer. The other thing I put in here is heart failure. Heart failure is a bit of a catch for us because it gives us sarcopenia, gives us ascites and it gives abnormal liver tests and it can give the peaches of cirrhosis and that's probably why I put that in there. But I’m not going to digress because I promise I will try and keep to time. So, using the history and I would say history, history, history and then using the examination and the liver test to help, you should be able to get an idea of what's going on really. And liver tests are a bit like an ECG. An ECG without the story is meaningless and liver tests without the story are meaningless. We know that not all liver test abnormalities reflect liver dysfunction (and hopefully you will have the image of that car in your mind), and in the correct setting maybe Albumin/Prothrombin time are better ideas of the functioning of the liver.

13.24 **Speaker:** So, the textbooks will tell us these things - that if you've got a hepatocellular damage, for example, in viral hepatitis, or in autoimmune hepatitis then the transaminases and the Bilirubin are raised. In cholestatic diseases things like gall stones, pancreas cancer, primary biliary cholangiopathy, drug induced cholestasis, then it's the alkaline phosphatase, the Bilirubin, I've snuck in the Gamma GT there as well. The Prothrombin can be up in both them because you'll remember that if you've got a blockage to your flow of bile you can't absorb vitamin K, which is one of the fat-soluble vitamins, so you get a slightly raised INR.

14.05 **Speaker**: So I’m not going to label this point because you probably all know this, but the rule of thumb that I’ve got if your ALT is up, it is going to be one of three things at a thousand.

* It's going to be shock, and that's quite common in the hospitals where people have had maybe sepsis and they've had hypoperfusion, they get acute tubular necrosis, they get acute liver ischemia and then you get an ALT that shoots up and shoots back down.
* Toxins. So probably the commonest thing we see in the hospital is paracetamol overdose. Your ALT can shoot up.
* The other thing then would be viral Hepatitis. So, things like Hepatitis A (you don't do you see an awful lot of that) Hepatitis E, CMV/EBV, Hepatitis B and occasionally Hepatitis C.

So those are the things you think about when they're up in the thousands. Then the commonest ones we see I suppose, and I mean we as in all of us in this seminar, would be in the ones maybe in the hundreds, and that's where the majority of the things lie:

* medication abnormality,
* not non-alcoholic fatty liver,
* alcohol related liver disease and stuff like.

Similarly, those that are just a couple of times the norm I don't ignore that, although I seem to have gone down in my tone of voice as I’ve gone from a thousand to a hundred to tens. Equally someone with an ALT of 40 needs it explained as much as someone with 400. But the time scale is important and the lovely graphs we now have in the Welsh Clinical Portal allow us to look at the chronology of things which is lovely. Saves drawing graphs.

15.45 **Speaker**: So, if I have someone with an abnormal liver test, I make no apology for doing a liver screen. The history is important, then the liver screen.

* So, I would do viral Hepatitis. You get A, B and C for nothing. In the right context if someone's got B then you may want to do D, but I wouldn't do that routinely. Hepatitis E is the commonest acute Hepatitis that I see. It classically affects middle-aged men. To do with probably unwashed vegetables or pork - it’s unclear and then in the right setting I would do CMV and EBV. I would note caution. I’ve come across two 40 year olds with acute CMV in the past two years and they were both people who'd married fairly young and then had marriage fallen apart and met new partners and obviously been exposed to a virus they had never seen, so that's interesting. But in general, EBV/CMV are picked up in late teenage/early twenties.
* Autoimmune disease is always common. It always trickles. You've always got a few people coming in and ANAs, liver antibodies they all come on the screen, immunoglobulins as well.
* Then there's the metabolic diseases you're all familiar with: Alpha 1, antitrypsin, hemochromatosis and again you always check for copper and ceruloplasmin, but the lab will cut off at about 40. It is as rare as hen’s teeth. I’ve got one woman in Llanelli I inherited and there was one who moved into the head injuries unit, but it is rare. I’m not going to talk about what's at the bottom of the slide there. I think I took that from another talk. That slide’s basically my whole job.

17.25 **Speaker**: So, with regards to alkaline phosphatase and cholestasis, I’ve put these little pictures on because I often say to the students ‘you've got to think of cholestasis from the top to the bottom’. We always think of the bottom. We think of head of the pancreas for cancer and stones. Yes, that caused it, but you've got to take it all the way back to the transporters. So, these are the little things that transport bile from the cell into the ducts and things like obstetric cholestasis and drug-induced cholestasis operate at that level. I don't know if you can see the arrow maybe you can but think of these cholestasis all the way from the top all the way down. Primary Biliary Cholangiopathy for example, is a small duct thing. But the outcome is the same - dark urine, pale stools, itching, jaundice. The commonest things of course, are stones and tumours, sadly. Again, the history is useful. What is interesting as well is that sometimes you get an acute viral Hepatitis and after you've gone through the viral, the ALT shoots up. As you start to improve, you go through a cholestatic phase. Sometimes you get some slightly cholestatic features. Presumably that's just the liver being unhappy.

18.31 **Speaker:** Part of the problem for you in primary care and for non-liver clinicians is that it's a really confusing field. You'll have gone through loads of talks like I’ve just talked about now about ALT and doing the liver screen and that's fine. But part of the problem is there's lots of different guidelines. It's often excessive. What you really want to know I guess is probably ‘What tests do you do before referring on?’

This is where my difficulty is. I don't know if there are any Hywel Dda GP's present, but I will often say ‘if you've got abnormal tests, just refer. I don't mind I’ll just see them.’ Now that is not something that I can say for all my colleagues across Wales. I’m very conscious of this. I don't know where you're from - presumably are all over. So, if i just say refer all your liver tests, I’m likely to get a real kicking at the next meeting!! So, there is guidance, but I accept it's confusing.

19.29 **Speaker:** I did a quick search now, because what you're asked to do is some of these rather poor non-invasive tests which are many, this is just a selection. I put a FibroScan at the top because that's the one I use. You've probably seen these things the ELF test, FIB4, BARD, the AST/ALT ratio, NAFLD score and APRI. These are all fairly straightforward. ELF is probably not straightforward because you need lots of weird things you can't get hold of. Well - P3NP is one of them. But the others you can do from the data that we've got to nickel or laboratory tests.

20.11 **Speaker:** I think it is confusing but I’m going to stick to the party line and I’m going to first go to the BSG guidance, which I think is in conjunction with the Royal College of General Practitioners. I hope this slide projects well because the ones for All-Wales does not project well. I’ve asked Nicola to send that out to you separately. I think basically they all say the same thing that history is important, and I would echo that. Again, you go into this pattern recognition and you know in many ways it's all right. If things are obvious, it's obvious isn't it but if they're not obvious then the patterns are less clear. I think what you will see is, if you suspect the person's got alcohol-related liver disease then you go to a different pathway. And again, that's confusing - you're already switched off. I don’t know if you are switched off, but I’m thinking ‘oh my goodness this is a load’. And then you go down the route of you know are the ASTs up? Right okay - let's get an ultrasound. Let's see how high it is. Do I need to repeat it? And I could talk you through the thing, but you've probably seen this all before and it does involve maybe looking at an AST or an ALT. I’m thinking oh this is hepatocellular damage and then going on to do the liver screen. Is it NAFLD? Are there risk factors for it? Let's do a score and then if it's not, let's do an ultrasound and to my mind and part of the problem I find - I know you can do this because anybody can do it, but how much time have you got to do this, is my concern. Which is why I’ve always said to my clinicians locally - if you've got abnormal liver tests just refer them. It's not a problem. I can do this. I think the problem with these scores is they're all right; they're not brilliant they're just all right. My personal feeling is that it's more of a sort of rationing service of who gets referred and who doesn't get referred. Anyway, I’m not going to get distracted.

**22.15 Speaker:** Looking at liver function, isolated Bilirubins, there's a whole thing on Gilbert Syndrome and then there's cholestasis looking for things but it's fairly straightforward. It’s a bit hard going. I downloaded the NAFLD one and this is where it becomes complicated or not complicated. I don't use any of the scores. I just use the FibroScan. So, when people come to me, I make a diagnosis and then I use the FibroScan as our risk stratification tool. I appreciate you don't have that in primary care, but I think these things are fine you know you can do a FIB4 test; you can do NAFLD things. They're all available on your phone, on MedCalc and they're all right. It gives you an idea of what's going on. I see some referrals coming through with these numbers on. I think if there's any concern or you're not happy, then I wouldn't have a concern. I suppose if you work in other parts of Wales you may wish to follow this pathway a bit better but the NAFLD one to be honest is the most common thing you're going to see and the most common thing I see in clinical practice.

23.26 **Speaker:** So, the other one is alcohol-related liver disease/alcohol related abnormal. We use this thing called the Audit-C. I’m not sure if you do. There's an abbreviated version which is quite useful and allows you to try out people and obviously refer on then to various tests and more importantly services which can support them. So, this guidance here, is what has come out from the BSG in about 2017/2018 and is on the RCGP website. I think there is a GP and I can't remember her name; she was involved with the BSG as part of this. They are good; they are very good. The only thing that worries me in primary care where to be honest staffing seems tricky, is how much time have you got to go through all this. I’m not sure. So, Wales have got one and you won't be able to read this, but I have asked Nicola or Hilary to send it out. It's got these QR codes on the side which are quite nice.

It gives you update but it basically says the same. I apologise for it being so awful to read but basically:

* take a history
* how high is it transaminase?
* do some scanning
* do some form of risk stratification and then
* refer on or just keep an eye on them in primary care

24.52 **Speaker:** So, I’m guessing, and it is a guess really, that the crux of the problem is ‘Oh my goodness - Which FibroScan? What do I do? Do I risk stratify? Do I just refer? These would be my questions if I was in primary care.

25.10 **Speaker:** The thing is, don't lose focus. The question is why are the liver tests abnormal? Do a history, do a screen, be aware a bit like liver test the non-invasive tests are not great (if you've got cirrhosis, they're good, if you haven't got cirrhosis, they're good. But the truth is that most people are in between and therefore they're not great. Even the FibroScan isn't great and even the liver biopsy isn't great. So, it's all about using what you've got. So, I think the ELF is very good, but we haven't got it available here. It involves hyaluronic acid and P3NP and some other thing. FibroScans are good and we can certainly do that for you. I don't just do a FibroScan because obviously as I’ve laboured, an assessment of liver tests involves history, examination, and tests. So, people often refer and say can you do a FibroScan? Well I can, but I’m not going to. I’m actually going to speak to the patient try and get a picture. The other things like the NAFLD score and FIP4 are fine. They're cheap, they're cheerful, they're easy to do, you don't need any fancy tests and they help guide. So, I think they're very reasonable and they help to build a picture

26.22 **Speaker:** So, in order to bring to a close, this part of the talk:

* Guidelines are important if nothing else they highlight the importance of not ignoring liver tests. When I first started as consultant, I went to a diabetes talk in Carmarthen. I was told by very senior GP ‘If I referred every abnormal living test to you, your clinic would be swamped’. Now that may be true but equally, how many people have got cirrhosis that weren't referred? So, I think I would rather have a swamped clinic and it becomes my problem and then people are not left having things unexplained in in primary care. So, it highlights the importance.
* I think clinical method stands, doesn't it? We learned it 30 years ago in medical school - history, history, history, and that is what's going to give you the most diagnosis. You've got a man coming in, he’s been an IV drug user, he's got a transaminase of 40 - well he's got chronic Hepatitis B/C until proven otherwise. It's not a judgment. It's using history and your knowledge.
* The liver screen is important. I do a liver screen on everybody. It's available on the Welsh Clinical Portal. You just go to Gastro Liver Screen and you get everything.
* Ultrasound is important as well.
* The other thing I think where we all get a bit tied up is written stratification because what do you do? Do these liver tests mean anything? So, a lot of people have just abnormal liver tests - a bit of fatty liver, but they are fine. They need lifestyle advice, they need risk factor managing (blood pressure, cholesterol, diabetes) but liver wise they're fine. So, we can use the FibroScan, we can use some of these non-invasive tests, but I really do feel that that crosses the interface between primary care and liver services. I’m more than happy to do that locally. Again, I don't think that can be replicated across Wales in certain hospitals which are big and busy. We may be a bit privileged down in the West. I think the strategy is because the number of liver tests is abnormal there is need for strategy and that's why hopefully Nicola’s emailed you or Blackboarded you those guidance that have come from the Wales Liver Panel.

**Speaker**: So, I don't know whether you want to stop there. Any questions?

28.34 **Q&A:** Why are we seeing more abnormal than normal passing through results?

I think the problem is that people are living longer, people are fatter and more metabolic, and I think more people are having medication. I think that's probably the issue with abnormal liver tests. I don't hold with this and this I’m sorry my I’m not having a go with you, but would you not treat somebody's blood pressure just because lots of people have high blood pressure? And that was my argument to a very senior GP in Carmarthen. Is it okay to ignore stuff? I don't think it is, but then I wouldn't, because this is my hobby horse. Do you stop treating blood pressure when you've treated 100, if there's 200? I think if this liver test is abnormal, it needs explaining. I mean otherwise, are you going to turn around to that patient in 20 years and say ‘I’m sorry, I didn't check it for Hep C because of there’s a cure for Hep C but oh well you know, it was quite busy’. So, I think if this abnormal liver tests it needs explaining.

29.47 **Q&A** Is there any benefit in repeating liver tests?

This is a really good question. I think it is on the guidance that you should repeat it. So, the story is if liver tests are up in primary care and they're up the second time, there's almost an 80 chance that they will stay up. It's very different in hospital practice, where people come in with sepsis or they're given drugs – liver tests often come up and down. I’ve had two recently on the Orthopaedic ward and I don’t know what they're doing there, but the alkaline phosphatase had gone up to about 6-700. But in primary care, if your liver tests are up and then you repeat them a couple months later and they're up, they're unlikely to go down. So yes, you're quite right. On that guidance which we can't read it does say to repeat it.

**Q&A:** We do need more funding and better liver services.

I agree with you. I don’t know where you work but certainly there is. There should be. There's an All Wales Liver Delivery Group and there's a Lead Liver Physician in every hospital in every health board.

We've got lots of money coming now, well not lots of money but there's liver nurses, there's FibroScan nurses, there's lots of things, but I think in a busy practice if you can do the basics I think that would help them. Again, I am conscious that you've got lots to do and the staff is tricky.

**Q&A** Mild fatty liver ultrasound and what would you recommend?

With regards to fatty liver this is a really important thing because this is the most common reason we're now seeing for end-stage liver disease. So, what I do with someone with a fatty liver and ultrasound I bring them in. I take a history. If it fits with fatty liver and it is fatty liver on the ultrasound and the liver screen is negative, we do a FibroScan. If the FibroScan is normal and they're quite old and we just give them lifestyle advice and get rid of them. If they are quite young and the FibroScan is normal I’d probably bring them back in about three years to make sure that it hadn't progressed and obviously if the FibroScan is abnormal, suggesting fibrosis, then obviously they get slotted into liver clinic. I guess in primary care your options are either to do those NAFLD score or the FIB4 score or to refer on. But I think it's not acceptable because the other reason – you can get fatty liver with alcohol, chronic Hepatitis C type 3 and so it's always worth explaining it. I think we all used to ignore it years ago. ‘You got a bit of fat on the liver, don't worry about it’. But I think we should worry about it along with all the things you've got to worry about in primary care postmenopausal bleeding and headaches and all the other stuff. I am conscious that this is my baby and you've got lots to do.

**Q&A:** Are there are consistent guidelines for timetable for repeating beyond three months for safety net?

I don't know. I think what the All Wales' Guidance says - we do it and repeat it in two months. I think once you've explained an abnormal liver test and you've done the risk stratification, there’s probably not much point in repeating it then because if it's abnormal it's going to be abnormal. I think that's probably what you're asking.

It's quite good this, because you can't come back to me as quickly, no hecklers!

47.52 **Q&A** Thanks for your presentation. We get a lot of slightly abnormal ALTs in primary care, if the flavour is a fatty liver due to obesity/diabetes I usually tend to have a good chat to the patient and try and reverse/optimize weight. Then repeat in three months. If coming down tend to just monitor, if going up I would tend to go for liver screening.

Well and that seems very reasonable. I think so what Jane is saying is that if it looks like fatty liver and it probably is, lifestyle intervention. So, if you've got fatty liver, the relative risk is 15 for dying of heart attack, stroke, diabetes, or related complications; your risk relative to your risk of dying of liver death is 2. So, if you are a betting person, you're going to die of a heart attack or a stroke with a fatty liver not liver failure. So, you're quite right - addressing the risk factors is the way forward. I think if things haven't changed and we think they probably won't change, then doing a screen and ultrasound seems particularly reasonable. I would add to that a non-invasive score, again depending on where you work

34.50 **Q&A** Thanks for your presentation. I have been seeing a few cases of incidental mildly raised transaminases with no clinical symptoms. When can we repeat?

I think repeating in about two to three months seems reasonable. Again, it's on that guidance which I can't read, it may even be less than that. But yes, these are the things you know slightly raised transaminases - you can't ignore them just in case it is something. The problem is Hep B is so treatable, Hep C is curable. You know you don't want to miss those things. Autoimmune Hepatitis is usually easier, but you can have disease with just slightly abnormal liver tests. Hemochromatosis is the other one isn't it, very very treatable.

35.40 **Q&A:** If ferritin or B12 is raised, ALT is normal, is it worth trying Haematology? Haematology say it's reactive/liver.

I think history is vital here. If people have got an unhappy liver from drinking or maybe fatty liver the ferritin can be up. In hemochromatosis you get high ferritin and high transferrin saturation so you're looking at levels. So, ferritin well over a thousand anyway and transferrin saturations 70, 80, 90%. You can sometimes see that in drinkers, but very rarely. The commonest picture is a high ferritin with a low transferrin saturation. I don't think I would perceive liver. I would certainly take a history and I think if there is something to support maybe a fatty liver or alcohol then an ultrasound would be reasonable. And it wouldn't be surprising that you'd find a fatty liver. It's worth noting that 50% of patients with fatty liver, have normal liver tests. There was quite a nice survey with Nottingham GPs (you may be aware) where we went in and looked at people who drank too much and I think people who had diabetes, and a lot of those had fatty liver irrelevant of their transaminases.

37.32 **Chair:** I think if you want to just go over a couple of the case studies, then we can come back to the questions at the side if there's still some time at the end.

37.50 **Speaker:** I don't know if there's any Gwendraeth Valley GPs? I’ve got nothing against the Gwendraeth Valley. My family were born and bred there. But there seems to be a rich picking on the liver front.

Case 1: This is a real case from a couple years ago. 70-year-old ex-miner from Trimsaran, came feeling and well for about a week. He felt nauseous, he was jaundiced.

The approach is to take a good history. Nothing really. Not a drinker. Tall and thin. Ex-miner. We did an ultrasound and we did some liver tests with the Bilirubin. So, he's got jaundice. He's got a hepatitis. Now you would remember earlier I said if the ALT is about a thousand or so, you think toxins, you think shock. Well he wasn't shocked. There were no obvious toxins in his medication, he hadn’t taken an overdose, so we think they have a viral hepatitis. So, in a man of this age Hep A is unlikely because he's probably either been immunised or he's had it as a child and he had acute Hepatitis E. The IGM and the PCR is positive. Surprisingly common. Part of the reason we don't pick it up is that the lab is a bit reluctant to do it unless you ask for it. There was a time they wouldn't do unless your ALT was over 500. But it's a common thing. Self-limiting disease. Can be troublesome in immune-suppressed people or in pregnant women. But quite a common disease. Certainly, more common clinically than Hepatitis A.

39.38 **Case 2:** 60-year-old woman, overweight presents with an infection, not septic. The ALT is a bit high, isn't it? Certainly, higher than I would expect for non-alcoholic fatty liver disease. Definitely higher than alcohol. She's presented with an infection. The history would really go along with - is this biliary sepsis? Prothrombin and Bilirubin is normal. The surgeons, oh gosh the surgeons ‘Oh the Bilirubin is normal, there's nothing going on.’ That's absolutely tosh! So, the number of people I’ve seen with gall stones with a normal Bilirubin. You know - surgeons! I hope there's no surgeons here.

Anyway, so this woman had an ultrasound. The common bile duct should be seven and was about nine but then the understanding again comes back. Well there's nothing there. Again, if the story is good and you think this woman's got biliary sepsis then go ahead and do an MRCP and that's what we did. So very often the ultrasound it's good but it doesn't show stones as commonly as we think. If there's any suspicion, I’ll do an MRCP and you often find stones lurking. So again, the history was what guided us there.

40.55 **Case 3:** So, a 25-year old drug abuser and drinker. Again, transaminase is normal. Well I don't know what the normal range is, but certainly I’ve said to you that a man should be about 30. So, the history is key here. He's got abnormal liver tests, he's been a drug abuser, he's got chronic Hepatitis C. Hep C is curable with two to three months of one tablet a day with a 95 to 100% cure rate.

41.28 **Case 4:** I’ve had a case like this very recently actually. Another girl from Pont Henry. She was 40. Just generally feeling unwell since Christmas. GP did a load of bloods because she was feeling unwell. ALT was 500. In this case, (the other lady had a positive ANA). Interestingly, IGGs and livers antibodies were negative, but the history was really good for autoimmune Hepatitis. So, a bit like this lady I’ve done the liver biopsy. Shows interface hepatitis. We've given a steroid on the day of the biopsy and within a week her transaminases are normal and she's feeling better. So again, you don't want to miss that because autoimmune Hepatitis responds so well to immunosuppression. If you miss it, it can proceed to cirrhosis at quite a pace.

So, I know it sounds like I’m being judgmental, but these are real cases. I think I’m going to just cobble them together.

42.20 **Case 5:** Young person. Found unwell. ALT is 2000 so it makes you think of toxins, Hepatitis, or shock. Well the patient's not shocked. Oh - they are shocked, actually. Low blood pressure. So, it could be a few things but the things to think about rehydrating the patient, reversing the shock but also because they're unwell, doing a Paracetamol level etc - that's more of a secondary care thing.

42.56 **Case 6:** This is also a secondary care thing. Since the ‘antibiotic police’ have stopped us using Co-amoxiclav. We've had a bit of a reprieve but Co-amoxiclav and some of the DOACs. Lots of antibiotics will cause drug induced liver injury. Very common. The Rheumatologist and the Dermatologist keep me practically in business with abnormal liver tests. Again, the history is key. Person in hospital, given antibiotics, turn yellow and you can see the graph. So, history is king there again.

43.30 **Speaker Summary**:

* Common liver tests are a poor reflection of real synthetic function.
* The alkaline phosphatases, ALKP, Gamma GT, Bilirubin are the commonest ones, but they've got lots of differentials why they're raised.
* Beware of what's normal. Some of the normal ranges may not be normal. Think of 18 and 30. Think of Club 18 to 30, that'll stick in your mind!
* Look for a pattern and take the history.
* Have a little checklist in your mind for what things you should look out for.

I do think that that's it then Nicola thank you.

44.06 **Chair:** I think there was just one extension to a question about the Hepatitis C current regime which you just mentioned, but asking can they be treated in primary care whilst awaiting an appointment?

44.20 **Speaker:** Scotland are about four million light years ahead of us. So, in Scotland and you're a drug taker you can go into a pharmacist have a finger prick test which tests you for PCR positive. That comes back in half an hour, you're then given a bag of antivirals and sent on your way. That's the level of what's going on in other places. The problem is they are really expensive. The drugs are like £20,00/£30,000. So that's part of the issue. They do tend to come out of secondary care, and they do tend to come on home care because we save the VAT. I’m not really answering your question. So, they could be treated in primary care but they're not. I think probably due to the price of the drugs. We do a bit of risk assessment; we check for other viruses and we do an ultrasound and we do a FibroScan. But- should they be vaccinated? Yes, they should be vaccinated as well. So, if you've got Hep C or if you've got cirrhosis we often recommend vaccinating because obviously if you get acute Hep A/B on top of your coexistent liver disease, you can run into trouble.

So, if you've got these, Twinrix is what we recommend, and you give these vaccines and the main thinking is that you don't get another insult on top of an unhappy liver.

46.00 **Chair:** Any last questions if you can pop them on the chat line now please. That seems to be it for now. Thank you very much Ian. I hope everybody feels somewhat clarified and we'll all refer to them as liver tests from now on.

I can just see the Doctor has just come back and is saying that she was meaning in healthy patients with no liver disease. Should they be recommended Hepatitis A/B vaccinations?

46.35 **Speaker:** No, I don't think so.

46.40 **Chair:** We've had another question in. What treatment would you give to a pregnant patient with Hep E?

45.45 **Speaker:** I don't know the answer to that because there's no specific treatment. I think it's more of a problem in other parts of the world, particularly around sort of flood plains e.g. Bangladesh area where they get lots of flooding. The answer is I don't know, I’m sorry. Certainly, in this country the treatment is supportive, and the disease is generally self-limiting except in people with immunosuppression and I am guessing now, whether there is some role for some of the anti-viral agents. But I don't know so I’m not going to say anything on that. Sorry.

**47.29 Chair:** Well thank you very much for your talk Ian. It’s certainly going to help me, and I’ll try not to send so many from the Amman/Gwendraeth Valley up to you now. Thank you very much.